81. (New) The isolated polypeptide of claim 80, wherein the polypeptide is a mammalian polypeptide.

82. (New) The isolated polypeptide of claim 81, wherein the mammalian polypeptide is a human polypeptide.

ADD E16

REMARKS

Shortened Statutory Period of Response under MPEP 809.02(a)

Applicant respectfully submits that MPEP 809.02(a) sets forth a 1-month (not less than 30 days) shortened statutory period for reply to a written requirement made without an action on the merit. The shortened statutory period for reply to the Office Action (Written Restriction) dated May 8, 2001 should be one month, *i.e.* June 8, 2001, which is the day that Applicant filed the response. Since May has 31 days, setting forth a response period of 30 days requires a response to be filed on June 7, 2001, which is improper because as stated above, MPEP 809.02(a) sets forth a 1-month shortened statutory period for reply to a written requirement made without an action on the merit. Thus, Applicant's response filed on June 8, 2001, to the Office Action dated May 8, 2001, is timely filed.

Status of the Claims

Claims 9-16, 39, and 40 have been cancelled. Claims 1-8, 19-38, 41-59 are withdrawn from consideration. New claims 77-82 are directed to compositions containing the polypeptide of claims 17, 18, 60, 61, 62, 63, 64, 65, 66, 67, 68, 69, 70 or 71. Accordingly, claims 17, 18, and 60-82 are currently before the Patent Office for examination.

Amendments to the Claims

Claims 17, 18, 60, 65-68, 70, and 73 have been amended to more clearly claim the subject matter of the invention. New claims 75 and 76 have been added.

Claim 17 has been amended to replace the word "thereof" with "of the polypeptide" to clarify that the fragments are fragments of the isolated polypeptide.

Claim 18 has been amended to delete the phrase "small molecule peptidomimetics thereof."

Support for the amendments to claims 60, 65-68, 70, and 73 and new claims 77-82 are summarized in Table 1. Respectfully, the amendments to claims 17, 18, 60, 65-68, 70, and 73 and the addition of new claims 77-82 do not add prohibited new matter.

Table 1

Claims	**Support in the Specification**
60	Page 52, lines 10-12 and lines 15-20
64, 65	Page 19, line 6
66	Page 51, line 22
67	Page 70, line 21
68, 70	Page 70, lines 26-30
74	Page 63, line 21; Figure 12
77, 78	Page 35, line 27; Page 36, line 17
79	Page 20, line 21; Page 35, lines 27-30
80	The hybridization and wash conditions are found on page 22, lines 7-19. The open reading frame of nucleotides 2811-2921, 3174-3283, 5158-5275 and 11955-12041 of SEQ ID NO: 35 is derived by comparing Figure 1D and page 57 (lines 20-26) which define the splice sites that produce the open reading frame of survivin to the sequence of SEQ ID NO: 35 and Figure 10. For instance, nucleotide 2811 is "A" of the ATG start codon set fort in Figure 10 (Page 2 of Figure 10). Nucleotide 2921 is the "G" residue which is the last nucleotide of the first exon described in Figure 1D ("2918GCG**G**|GTGAG"). Nucleotide 3174 refers to the A residue which is the first nucleotide of the second exon described in Figure 1D ("3161CTGTCCCTTGCAG|**A**TGGC"). Nucleotide 3283 is the "T" residue which is the last nucleotide of the second exon described in Figure 1D ("3280CCA**T**|GTAAG"). Nucleotide 5158 refers to the A residue which is the first nucleotide of the third exon described in Figure 1D ("5145TTATTTTCTAG|**A**GAGG"). Nucleotide 5275 is the "T" residue which is the last nucleotide of the third exon described in Figure 1D ("5272AA**T**T|GTATG"). Nucleotide 11955 refers to the G residue which is the first nucleotide of the fourth exon described in Figure 1D ("11942TCTTTATTTCCAG|**G**CAAA"). Lastly, nucleotide 12041 is the last nucleotide before the stop codon of survivin (see Figure 10A and 10B).
81, 82	Page 6, lines 14-27; Figure 2

Rejection under 35 U.S.C. § 112, Second Paragraph

Claims 60, 64-70, 73, and 75 stand rejected under 35 U.S. C. § 112, second paragraph, as being indefinite.

Applicant has amended claims 60, 64-70, and 74 to more clearly claim the subject matter of the claimed invention. Accordingly, this rejection has become moot.

Rejections under 35 U.S.C. § 112, First Paragraph

A. Claims 39, 40, and 72 stand rejected under 35 U.S.C. § 112, first paragraph, as being drawn to vaccines which are purportedly not enabled by the specification.

Applicant has cancelled claims 39 and 40. Accordingly, the rejection of claims 39 and 40 has become moot.

Applicant respectfully submits that claim 72 is directed to a fusion protein and not to a vaccine. Survivin fusion proteins, as shown in Example 3, can be used to generate monoclonal antibodies. As described on page 21, lines 15-18 of the specification, survivin antibodies are useful for the detection of survivin, the purification of survivin, and for modulating survivin binding to its partner. Additionally, the fusion protein can be used to isolate survivin binding partners, purify survivin antibodies, and modulate the binding of survivin to its partner.

Accordingly, Applicant requests withdrawal of this rejection.

B. Claim 18 stands rejected under 35 U.S.C. § 112, first paragraph, as encompassing conservatively substituted homologs of SEQ ID NO: 4, and small molecule peptidomimetics of SEQ ID NO: 4, which are purportedly not enabled by the specification.

Applicant respectfully submits that the phrase "small molecule peptidomimetics" has been deleted from the claim. Thus, the rejection with respect to this part of the claim has become moot.

With respect to conservatively substituted homologs of SEQ ID NO: 4, Applicant respectfully points out that conservatively substituted homologs are polypeptides with amino acid alterations that do not affect the functional activity of survivin such as binding to its partner or inhibiting cellular apoptosis (page 18, line 11). The specification provides guidance to make and/or isolate variants, including conservatively substituted variants, and screen for the described functions. For example, page 44, line 25 through page 46, line 13 disclose examples of assays for promoting apoptosis. Additionally, the specification provides the nucleic acid encoding survivin

and Example 1 discloses isolation of survivin which are applicable to isolation of variants. Moreover, conservative amino acids are well known, it is within the skill of the artisan to obtain conservatively substituted polypeptides comprising SEQ ID NO: 4. Further, Example 18, lines 17-25 disclose the functional importance of SEQ ID NO: 4 and provide methods of using SEQ ID NO: 4. Accordingly, given the guidance provided by the specification, it would not require undue experimentation to obtain conservative homologs comprising SEQ ID NO: 4. Thus, Applicant requests withdrawal of this rejection.

C1. Claim 73 stands rejected under 35 U.S.C. § 112, first paragraph, as drawn to a fusion protein comprising an unspecified fragment of SEQ ID NO: 34 with a C-terminal ring finger protein, which, according to the Office Action, is not enabled by the specification.

The Office Action alleges that the survivin chimeric molecule comprising a C-terminal ring-finger domain was found to be inactive at inhibiting apoptosis. Applicant respectfully submits that the survivin fusion protein comprising a C-terminal ring finger inhibits apoptosis almost as well as wild-type survivin (see figure 12).

Also, Applicant respectfully points out that the specification teaches various ways of using the presently claimed survivin fusion proteins. Survivin fusion proteins are useful for generating antibodies that can detect the presence of survivin or modulate survivin binding to its target and for isolating survivin binding partners, purifying survivin antibodies, and modulating the binding of survivin to its binding partner. Thus, even if the survivin peptide fusion proteins do not inhibit apoptosis, the skilled artisan would be able to use them in an alternative manner taught by the specification. Accordingly, Applicant requests withdrawal of this rejection.

C2. Claims 64-68 and 70 stand rejected under 35 U.S.C. § 112, first paragraph, as being enabling according to the Office Action only for fragments consisting of 20 amino acids of SEQ ID NO: 4, 40 amino acids of the BCOOH domain, and 70 amino acids of the BIR domain.

As discussed above, the specification provides various methods for using survivin peptides. Inhibition of apoptosis is only one of the methods for using survivin peptides. It is within the skill of the artisan to use survivin peptides to generate antibodies. The skilled artisan routinely generates antibodies using 10, 15, and 17 amino acid peptides. In fact, Example 2 specifically teaches generation of a survivin antibody using a survivin peptide of 17 amino acids.

As shown in Example 5, the survivin antibody generated in Example 2 is useful for detecting the presence of survivin in various tissues. Thus, even when the peptides of 10, 15, and 17 amino acids may not be useful for inhibiting apoptosis, they are useful for generating antibodies which may be used in different ways as discussed above.

Rejection under 35 U.S.C. § 102(e)

Claims 17, 60, and 61 stand rejected under 35 U.S.C. § 102(e) as being anticipated by Korneluk *et al.* (U.S. Patent 6,107,041).

Applicant respectfully submits that the human IAP proteins disclosed by Korneluk are 500 to 620 amino acids in length and having a molecular weight of about 55 KDa. The survivin polypeptide having SEQ ID NO: 34 has only 142 amino acids and a molecular weight of 16.5 KDa as determined by SDS PAGE. The human IAP proteins are not allelic variants of the presently claimed polypeptide having SEQ ID NO: 34.

Moreover, it is pointed out that the Korneluk does not disclose peptides of SEQ ID NO: 34. In col. 1, line 40, Korneluk describes human IAP proteins as comprising two N-terminal domains with each domain consisting a 70 amino acid repeat motif. Korneluk does not disclose a human IAP peptide having 70 or 140 amino acids. Further, Korneluk does not disclose a human IAP peptide having a fragment of SEQ ID NO: 34. Thus, the polypeptides disclosed in Korneluk do not meet the structural limitations of the claims. Applicant request withdrawal of this rejection.

Conclusion

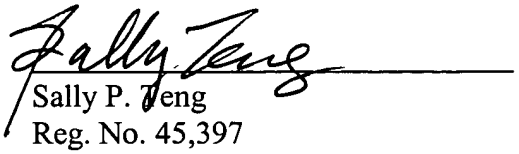
In view of the amendments and accompanying remarks, Applicant respectfully requests reconsideration and timely allowance of the pending claims. Should the Examiner feel that there are any issues outstanding after consideration of this response, the Examiner is invited to contact Applicant's undersigned representative to expedite prosecution.

If there are any other fees due in connection with the filing of this response, please charge the fees to our Deposit Account No. 50-0310. If a fee is required for an extension of time under 37 C.F.R. § 1.136 not accounted for above, such an extension is requested and the fee should also be charged to our Deposit Account.

Respectfully Submitted,

MORGAN, LEWIS & BOCKIUS LLP

Dated: January 30, 2002

By: 
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VERSION WITH MARKINGS TO SHOW CHANGES MADE

In the Claims:

Claim 17 has been amended as follows:

17. (Twice Amended) An isolated polypeptide comprising the amino acid sequence as set forth in SEQ ID NO: 34, allelic variants **of the polypeptide** [~~thereof~~], and fragments **of the polypeptide** [~~thereof~~] that retain the ability to inhibit cellular apoptosis.

Claim 18 has been amended as follows:

18. (Twice Amended) A polypeptide comprising the sequence EGWEPDDDPIEEHKKHSSGC (SEQ ID NO: 4), and its conservatively substituted homologs [~~and small molecule peptidomimetics thereof~~].

Claim 60 has been amended as follows:

60. (Amended) An isolated mammalian polypeptide of the IAP family, wherein the polypeptide has a molecular weight of 16.5 KDa as **determined by SDS PAGE** and inhibits apoptosis.

Claim 64 has been amended as follows:

64. (Amended) An isolated polypeptide comprising at least 10 **contiguous** amino acids of SEQ ID NO: 34.

Claim 65 has been amended as follows:

65. (Amended) An isolated polypeptide comprising at least 15 **contiguous** amino acids of SEQ ID NO: 34.

Claim 66 has been amended as follows:

66. (Amended) An isolated polypeptide comprising at least 17 **contiguous** amino acids of SEQ ID NO: 34.

Claim 67 has been amended as follows:

67. (Amended) The polypeptide of claim 64, wherein the polypeptide comprises at least 20 **contiguous** amino acids of SEQ ID NO: 34.

Claim 68 has been amended as follows:

68. (Amended) The polypeptide of claim 64, wherein the polypeptide comprises at least 40 **contiguous** amino acids of SEQ ID NO: 34.

Claim 70 has been amended as follows:

70. (Amended) The polypeptide of claim 64, wherein the polypeptide comprises at least 70 **contiguous** amino acids of SEQ ID NO: 34.

Claim 74 has been amended as follows:

74. (Amended) A mutant polypeptide comprising an amino acid sequence that differs from SEQ ID NO: 34 in that one or more amino acids in SEQ ID NO: 34 is substituted with another amino acid, wherein the one or more residues are selected from the group consisting of Arg^{18}, Phe^{22}, Trp^{25}, Pro^{26}, Pro^{35}, Ala^{39}, Ala^{41}, Gly^{42}, Cys^{46}, Asp^{53}, Cys^{57}, Cys^{60}, Leu^{64}, Trp^{67}, Pro^{69}, Asp^{71}, Asp^{72}, **Pro^{73}**, His^{77}, and Cys^{84}.